

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

The application has been amended as follows:

In the specification, at page 19, lines 19-29, please delete the existing paragraph and replace with the following, amended paragraph:

In contrast, anti-aminophospholipid antibodies, bispecific antibodies, and antigen binding fragments thereof, that are conjugated to, or operatively associated with, cytotoxic or anticellular agents are referred to herein as "anti-aminophospholipid immunotoxins". Likewise, anti-aminophospholipid antibodies, bispecific antibodies, and antigen binding fragments thereof, that are conjugated to, or operatively associated with, coagulation factors are herein referred to as "anti-aminophospholipid coaguligands". The use of anti-aminophospholipid immunotoxins and anti-aminophospholipid coaguligands in tumor treatment is also contemplated by the present inventors and is disclosed and claimed in first and second provisional applications Ser. No. 60/092,589 (filed Jul. 13, 1998) and Ser. No. 60/110,600 (filed Dec. 2, 1998) and in co-filed U.S. and PCT patent application (~~Attorney Docket Nos. 4001.002300, 4001.002382, 4001.002383 and 4001.002210~~) Ser. No. 09/351,457, now U.S. Pat. No. 6,132,694; Ser. No. 09/351,598, Ser. No. 09/351,149 and WO 00/02584, each specifically incorporated herein by reference.

In the specification, at page 58, line 20 to page 59, line 2, please delete the existing paragraph and replace with the following, amended paragraph:

The present aminophospholipid tumor vasculature expression studies further support the use of coaguligands directed against known tumor vasculature markers as selective thrombotic agents for the treatment of solid tumors. The present observations also led the inventors to develop further tumor treatment methods. For example, the use of anti-aminophospholipid immunotoxins and anti-aminophospholipid coaguligands in tumor treatment is disclosed and claimed in first and second provisional applications Ser. No. 60/092,589 (filed Jul. 13, 1998) and Ser. No. 60/110,600 (filed Dec. 02, 1998) and in co-filed U.S. and PCT patent application (~~Attorney Docket Nos. 4001.002300, 4001.002382, 4001.002383 and 4001.002210~~) Ser. No. 09/351,457, now U.S. Pat. No. 6,132,694; Ser. No. 09/351,598, now U.S. Pat. No. 6,818,213, Ser. No. 09/351,149, now U.S. Pat. No. 7,067,109 and WO 00/02584, each specifically incorporated herein by reference. The surprising discovery of stable PS expression on intact tumor-associated endothelial cells, which are not

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undergoing cell death, renders such methods both practicable and surprising (given that PS expression was thought to be associated only with cell destruction).

In the specification, at page 113, lines 9-18, please delete the existing paragraph and replace with the following, amended paragraph:

The present invention further provides combined tumor treatment and imaging methods, based upon anti-aminophospholipid binding ligands. Anti-aminophospholipid binding proteins or antibodies that are linked to one or more detectable agents are envisioned for use in pre-imaging the tumor, forming a reliable image prior to the treatment, which itself targets the aminophospholipid markers. In addition to antibodies, the use of detectably labeled annexins and other aminophospholipid binding ligands is contemplated, as disclosed and claimed in first and second provisional applications Ser. No. 60/092,589 (filed Jul. 13, 1998) and Ser. No. 60/110,600 (filed Dec. 2, 1998) and in co-filed U.S. and PCT patent application (~~Attorney Docket Nos. 4001.002300, 4001.002382, 4001.002383 and 4001.002210~~) Ser. No. 09/351,457, now U.S. Pat. No. 6,132,694; Ser. No. 09/351,598, now U.S. Pat. No. 6,818,213, Ser. No. 09/351,149, now U.S. Pat. No. 7,067,109 and WO 00/02584, each specifically incorporated herein by reference.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRANDON J. FETTEROLF whose telephone number is (571)272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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